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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,876	01/16/2003	Jason Peter Brown	A0000180/2-01-MG	4968

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EXAMINER

CHANDRA, GYAN

ART UNIT	PAPER NUMBER
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1646

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/088,876

Applicant(s)

BROWN ET AL.

Examiner

Gyan Chandra

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 July 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,5-14,18-20,22,35 and 54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5-14,18-20 and 35 is/are rejected.
- 7) ☐ Claim(s) 2, 22 and 54 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

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Re: Brown et al.

Date of priority: 09/16/1999

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The amendment filed on 7/20/2006 has been entered.

The amendments of claims 1-2, 5-14, 18-20, 22 and 35 have been made of record.

The addition of new claim 54 and the cancellation of claims 3-4, 15-17, 21, 23-34, and 36-53 are acknowledged.

Claims 1-2, 5-14, 18-20, 22, 35 and 54 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

It is noted that this application appears to claim subject matter disclosed in prior Application No. 09/397,550, filed on 9/16/1996 and the PCT/EP009137 filed on 9/18/2000. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Response to Arguments

Applicant's arguments, see Remarks, filed 7/20/2006, and the amendments with respect to the rejection(s) of claim(s) 1-5 under 35 USC 102 (e) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Brown et al (IDS, 1998).

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-14, 18-20, 35 and 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7, 8, 9, 19, 35 and 54, recite a symbol " δ " for a subunit of the instantly claimed channel subunit is " $\alpha_2\delta_2$ ". This renders the claim(s) indefinite because it is not clear how a " δ " can be derived from the subunit " $\alpha_2\delta_2$ ". Therefore, the metes and bounds of the claimed invention cannot be determined.

Claims 5-6, 10-14, 18, and 20 are rejected for being directly or indirectly depend from a broad and indefinite claim. Therefore, the metes and bounds of the claimed invention cannot be determined.

Claim 1 recites the limitation "its δ " in 1(b) lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 19 recites the limitation "its δ " in lines 3, 4 and 5. There is insufficient antecedent basis for this limitation in the claim.

Claim 35 recites the limitation "its δ " in lines 2 and 3. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5-14, 18-20, and 35 are rejected under 35 U.S.C. 103(a) as being obvious over Lerman et al (previously presented, US Patent No. 6,441,156) in view of Brown et al (IDS, J. Biol. Chem. 273: 25458-25465, 1998).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer

in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claims 1, 5-14, 18-20, and 35 are broadly drawn to a calcium channel $\alpha_2\delta_2$, wherein it is soluble and retains the functional characteristics of the full length or wild type subunit from which it derives, wherein its δ peptide (is being interpreted as δ_2) has C-terminal deletion, wherein in its α_2 peptide comprises at least the ligand interacting part(s) (claim 1), wherein the full-length is naturally expressed in the cerebral cortical (claim 5), wherein the full-length $\alpha_2\delta_2$ subunit from which it derives is voltage dependent (claim 6), wherein the $\alpha_2\delta_2$ subunit is cleaved (claim 7), wherein the $\alpha_2\delta_2$ subunit is cleaved into separate α_2 and δ_2 peptides, and α_2 and δ_2 peptides are disulfide bridged (claim 8-9), wherein the $\alpha_2\delta_2$ subunit is not cleaved (claim 10), wherein the $\alpha_2\delta_2$ subunit is purified or isolated, and that the $\alpha_2\delta_2$ subunit is characterized in that it is processed as the full-length subunit (claims 11-12), wherein the $\alpha_2\delta_2$ subunit is producible or produced by a baculovirus/insect cells expression system, wherein said calcium channel interacts with ligand gabapentin (claim 18), wherein the $\alpha_2\delta_2$ subunit does not comprise a part of the transmembrane domain of the full-length subunit from which it derives which renders said calcium channel insoluble (claim 19), and wherein the full-length $\alpha_2\delta_2$ subunit from which it derives is $\alpha_2\delta$ -2 subunit (claim 20).

Lerman et al teach cloning and expression of a full-length calcium channel $\alpha_2\delta$ -2. Lerman et al teach that the expression subunit $\alpha_2\delta$ -2 in *Xenopus* oocyte provides

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current-voltage relationship (col.6 under Brief description, FIG. 3 and FIG.4 and col. 13, lines 54+). Lerman et al contemplate expressing said polypeptide using baculovirus expression vector in insect cells (col. 27, line 59+). Lerman et al teach that the calcium channel $\alpha_2\delta$ -2 is expressed in whole brain, which is inclusive of cerebral cortex (see a northern blot tested positive comprising tissues e.g., thalamus, subthalamic nucleus, substantia nigra, whole brain, hippocampus, corpus collosum, caudate nucleus, and amygdala) (col. 44, lines 24+). Lerman et al teach that the calcium channel $\alpha_2\delta$ -2 and another calcium channel $\alpha_2\delta$ -1 (previously known as $\alpha_2\delta$; see col.16, line 56) share similar overall secondary structure (col. 42, lines 18+). Lerman et al refer to Brown et al, 1985) for describing characteristics of $\alpha_2\delta$ -1 subunit of a calcium channel (col. 17, lines 35, lines 62+) which is a voltage dependent calcium channel. Lerman et al teach that the subunit $\alpha_2\delta$ is cleaved post-translationally and that the peptides α_2 and δ are linked with disulfide bond (col. 17, lines 31+). Lerman et al a single transmembrane domain in the δ subunit that anchors $\alpha_2\delta$ subunit with the membrane (col.17, lines 33+). Lerman et al suggest making fusion proteins to have the calcium channel $\alpha_2\delta$ -2 in soluble form (col. 28, lines 11+). Lerman et al teach that the subunit $\alpha_2\delta$ has a high affinity binding for the drug gabapentin (col. 17, lines 61+).

Lerman et al do not teach that the $\alpha_2\delta$ -2 is not cleavable. Lerman et al do not explicitly teach that the deletion of C-terminal of $\alpha_2\delta$ -2 subunit will make protein soluble.

Brown et al teach cloning and deletion mutagenesis of the $\alpha_2\delta$ calcium channel subunit from porcine. Brown et al teach that a deletion lacking putative membrane anchor in the δ sequence was found to be both membrane associated and soluble

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secreted form (abstract). Brown et al teach that the soluble form of the $\alpha_2\delta$ calcium channel subunit was not proteolytically cleaved into separate α_2 and δ peptides but still retained the ligand interacting part(s) as it retains a high affinity binding for [3H]gabapentin. Brown et al teach various deletions showing portion of the $\alpha_2\delta$ calcium channel subunit responsible for [3H]gabapentin binding.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make various deletions as taught by Brown et al in the calcium channel $\alpha_2\delta$ -2 of Lerman et al to obtain soluble $\alpha_2\delta$ -2 calcium channel for methods of rational drug design as described by Lerman et al (col.32, lines 66-67 and col.33, line 1). Further, one would have been motivated to do so because Lerman et al refer to Brown et al for the details of cloning and ligand binding studies in which Brown et al teach that C-terminal deletion of the polypeptide would allow one of skill in the art to achieve a large scale protein production in soluble form and further, Brown et al teach that the soluble form of protein was not proteolytically cleaved which would provide benefit in screening assays because it retains the ligand interacting part(s). Additionally, one would have a reasonable expectation of success as Lerman et al teach that the calcium channel $\alpha_2\delta$ -2 and the $\alpha_2\delta$ calcium channel taught by Brown et al are structurally similar and that Brown et al teach various deletions and mutations that make the $\alpha_2\delta$ calcium channel protein soluble while retaining at the ligand interacting part(s) of the full-length subunit from which it derives.

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Claims 2, 22 and 54 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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